

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

CLAIMS

5 1. An oligonucleotide comprising from about 2 to about 100 nucleotides and containing at least one unmethylated CpG dinucleotide.

10 2. The oligonucleotide of claim 1 which is represented by the following formula:



15 wherein C and G are unmethylated,  $\text{X}_1$ ,  $\text{X}_2$ ,  $\text{X}_3$  and  $\text{X}_4$  are nucleotides and a GCG trinucleotide sequence is not present at or near the 5' and 3' termini.

15 3. The oligonucleotide of claim 2 having a phosphate backbone modification.

20 4. The oligonucleotide of claim 3 wherein the phosphate backbone modification is a phosphorothioate backbone modification.

25 5. The oligonucleotide of claim 4 comprising the following nucleotide sequence:

5' GGGGTCAACGTTGAGGGGGG 3' (SEQ ID NO:1)

30 6. The oligonucleotide of claim 5 having a phosphate backbone modification.

30 7. The oligonucleotide of claim 6 wherein the phosphate backbone modification is a phosphorothioate modification.

35 8. An oligonucleotide delivery complex comprising the oligonucleotide of claim 1 and a targeting means.

35 9. An oligonucleotide delivery complex of claim 8, wherein the targeting means is selected from the group consisting of cholesterol, virosome, liposome, lipid, a target cell specific binding agent

10. A pharmaceutical composition comprising the oligonucleotide of claim 9 and a pharmaceutically acceptable carrier.
- 5           11. A pharmaceutical composition comprising the oligonucleotide of claim 2 and a pharmaceutically acceptable carrier.
- 10           12. A method for activating a subject's B cells comprising contacting the B cells with an effective amount of the oligonucleotide of claim 1.
- 15           13. A method for activating a subject's B cells comprising contacting the B cells with an effective amount of the oligonucleotide of claim 2.
- 20           14. A method for activating a subject's natural killer cells comprising contacting the natural killer cells with an effective amount of the oligonucleotide of claim 1.
- 25           15. A method for activating a subject's natural killer cells comprising contacting the natural killer cells with an effective amount of the oligonucleotide of claim 2.
- 30           16. A method for treating, preventing or ameliorating an immune system deficiency in a subject comprising administering to the subject an effective amount of a pharmaceutical composition of claim 10.
- 35           17. A method for treating, preventing or ameliorating an immune system deficiency in a subject comprising the steps of:
- a) contacting lymphocytes obtained from the subject with a composition of claim 1 ex vivo, thereby producing activated lymphocytes; and
- b) readministering the activated lymphocytes obtained in step a) to the subject.
18. A method for vaccinating a subject comprising administering to the subject a composition of claim 10 in conjunction with administration of a vaccine.

- 5            19. A method for treating a disease associated with an immune system activation in a subject comprising administering to the subject an effective amount of a neutral oligonucleotide alone or in conjunction with a pharmaceutically acceptable carrier.
- 10            20. A method of claim 19 wherein the disease associated with immune system activation is systemic lupus erythematosus.
- 15            30. A method of claim 19 wherein the disease associated with immune system activation is sepsis.
- 20            31. An improved method for performing antisense therapy comprising methylating CpG containing oligonucleotides prior to administration to a subject.
- 25            32. An improved method for in vivo diagnoses using oligonucleotide probes comprising methylating CpG containing oligonucleotides prior to administration to a subject
- 30            33. An oligonucleotide which is capable of interfering with the activity of viral or cellular transcription factors and containing a consensus immunoinhibitory CpG motif represented by the formula:
- 5' GCGX<sub>n</sub>GCG3'
- wherein X = a nucleotide and n = in the range of 0-50.
- 35            34. An oligonucleotide of claim 33, wherein X is a pyrimidine.
- 30            35. An oligonucleotide of claim 34, wherein X<sub>n</sub> is a CpG dinucleotide
- 35            36. A method for treating or preventing a viral infection in a subject comprising administering to the subject an immunoinhibitory oligonucleotide of claim 33.